Assessment of Arginine - Glycine - Aspartic acid (RGD) Functionalized Hydrogel Mixed with Xenograft for Vertical Alveolar Ridge Augmentation Using a Computer Guided Sandwich Osteotomy Technique

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Abstract

Background: Vertical alveolar ridge augmentation remains a challenging procedure in implant dentistry. Computer guided sandwich osteotomy technique (CGSOT) preserves vascularity of the mobilized segment and allows simultaneous implant placement with high precision and time saving. Recently, RGD-functionalized hydrogels have attracted attention due to their ability to enhance cellular adhesion and osteogenic activity. This study evaluated the effect of adding RGD-functionalized hydrogel to xenograft using computer-guided sandwich osteotomy for vertical ridge augmentation.

patients and Methods: Twenty-four patients presenting with maxillary vertical ridge deficiencies of 4–8 mm were enrolled in this randomized controlled clinical trial and allocated into two equal groups (n = 12). The control group received computer-guided sandwich osteotomy with simultaneous implant placement, xenograft, and collagen membrane, whereas the study group received the same treatment protocol with RGD-functionalized hydrogel mixed with xenograft. Volumetric bone changes were assessed using CBCT-based segmentation analysis with Mimics Medical 21.0 software at baseline, immediately postoperatively, and after 6 and 12 months. Statistical analysis was performed at a significance level of $p \leq 0.05$.

Results: Both groups demonstrated significant volumetric bone gain compared with baseline values ($p < 0.05$). In the control group, mean bone volume increased from 3.19 ± 0.89 cm³ preoperatively to 5.39 ± 1.01 cm³ after 12 months. In the study group, bone volume increased from 3.54 ± 0.62 cm³ to 5.13 ± 0.72 cm³ after 12 months. The augmented volumes were largely maintained throughout the follow-up period in both groups. No statistically significant differences were observed between groups at any evaluation interval ($p > 0.05$). However, significant time-related changes were detected within each group.

Conclusions: Computer-guided sandwich osteotomy combined with simultaneous implant placement is an effective technique for the management of maxillary vertical ridge deficiencies and provides stable volumetric bone augmentation over a 12-month period. The patient-specific guide resists the tension generated by the palatal soft tissues, thereby preventing palatal rotation and tipping of the transported segment. RGD-functionalized hydrogel mixed with xenograft achieved favorable regenerative outcomes; it did not provide a significant volumetric advantage over xenograft alone.

Keywords: Vertical ridge augmentation; Sandwich osteotomy; Computer-guided surgery; RGD hydrogel; Xenograft; Dental implants; Bone regeneration.

How to cite this article: Morsi AK, Madany UM, Abozaid HM. Assessment of Arginine - Glycine - Aspartic acid (RGD) Functionalized Hydrogel Mixed with Xenograft for Vertical Alveolar Ridge Augmentation Using a Computer Guided Sandwich Osteotomy Technique. Int J Drug Deliv Technol. 2026;16(63s): 1944-1950. DOI: 10.25258/ijddt.16.63s.200

Introduction

Vertical alveolar ridge augmentation (VRA) remains one of the most challenging procedures in dental implant because bone gain must occur in the absence of natural osseous wall containment.[1] Although several techniques have been proposed for the reconstruction of vertically deficient ridges, including guided bone regeneration (GBR), distraction osteogenesis, and bone block grafting, these

approaches are often technique sensitive and may be associated with donor site morbidity, multiple surgical interventions, prolonged treatment time, and increased cost. Consequently, the search for predictable and minimally invasive alternatives for VRA continues.[2]

The sandwich osteotomy technique (SOT) has emerged as a valuable option for the treatment of vertical alveolar ridge deficiencies. The technique involves mobilization of an alveolar bone segment through one horizontal and two vertical osteotomies, followed by placement of an interposition graft. Preservation of the vascular supply to the mobilized segment promotes favorable healing and allows simultaneous implant placement, thereby reducing overall treatment duration.[3] However, a major limitation of SOT is the potential rotation and tipping of the transported segment caused by soft tissue tension, particularly in the maxilla, which may compromise the amount and predictability of vertical bone gain.[4] Recently, computer-guided surgery has been introduced to improve the accuracy of osteotomy design, segment mobilization, and implant positioning, potentially enhancing the predictability of the procedure.[5]

In parallel, advances in biomaterials have encouraged the use of bone substitutes as alternatives to autogenous grafts. Xenografts are widely used because of their excellent space maintaining properties and ability to minimize postoperative dimensional shrinkage.[6] Nevertheless, their low resorption rate may limit new bone formation by occupying space within the regenerated area. To overcome these limitations, bioactive materials capable of enhancing cellular activity and tissue regeneration have gained increasing attention.[7]

Hydrogels represent a promising class of regenerative biomaterials due to their high-water content, biocompatibility, and ability to conform to irregular defect geometries.[8] Among these materials, peptide-functionalized hydrogels incorporating the Arg-Gly-Asp (RGD) sequence have demonstrated significant potential in tissue engineering. The RGD peptide is a well-established cell-adhesion motif that promotes integrin-mediated cellular attachment, proliferation, differentiation, and extracellular matrix formation, thereby enhancing tissue regeneration and bone healing.[9] Therefore, the present study aimed to evaluate the effect of adding RGD-functionalized hydrogel to xenograft on bone augmentation in vertically deficient ridges treated with computer-guided sandwich osteotomy and simultaneous implant placement.

Patients and Methods

This randomized controlled clinical trial included 24 patients with age ranging between 30 to 45 years old were recruited from the outpatient clinic of the Department of Oral Medicine, Periodontology, Oral Diagnosis and Oral Radiology, Faculty of Dental Medicine, Al-Azhar University, Cairo, Egypt. Patients included in the study have maxillary vertical ridge deficiencies of 4–8 mm according to the Cologne Classification of Alveolar Ridge Defects (CCARD)[10] with good oral hygiene. Excluding patients with systemic conditions which are generally considered a contraindication to implant surgery, Pregnant or lactating females, smokers, patient treated by immunosuppressive chemotherapy or radiotherapy and allergy to any material or medication used in the study. The study protocol was approved by the institutional ethics committee (Approval No. 946/2826) and registered at ClinicalTrials.gov (NCT07028606).

The patients were randomly assigned into two equal groups (n = 12) either control group or study group using computer generated randomization (www.randomizer.org). The control group received computer-guided sandwich osteotomy with simultaneous implant placement, xenograft, and collagen membrane, whereas the study group received the same treatment protocol with the addition of RGD-functionalized hydrogel mixed with the xenograft.

Preoperative assessment included clinical evaluation of keratinized tissue thickness and width, as well as CBCT with minimal field of view for analysis defect characterization and treatment planning.

Guide fabrication

Precise osteotomies and implant position were established through fabrication of two digital surgical guides for each patient; four steps were performed. First: preoperative CBCT was uploaded to bone segmentation module (Anatomica Ai Software)[1] for osteotomy guide fabrication followed by implant simulation module for implant planning. Second: preforming intraoral digital scanning using Rainbow

[1] An AI-powered digital dentistry platform focused on implant planning, guided surgery, intraoral scanning, and restorative workflows. Atlanta, Georgia, USA.

Scanner Prime (Dentium, Suwon, Korea)[2] and exported as standard tessellation language (STL) files. (Figure 1-2) Third: STL files were imported to Anatomica Ai software and superimposed on Digital Imaging and Communications in Medicine (DICOM) files, for image registration based on the teeth matching. Fourth: after surgical guides designing and virtual planning either for osteotomies or implant guide. The guides were exported as STL format file and printed using (SLA) technology with clear resin.

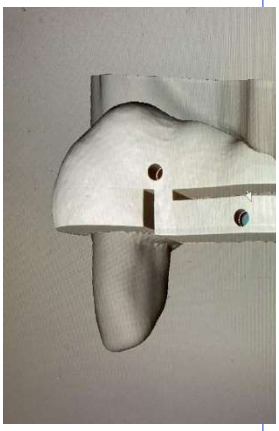


Figure 1 STL file exported from Anatomica Ai software as virtual design of the first guide aims to mark position of the three full-thickness osteotomies.

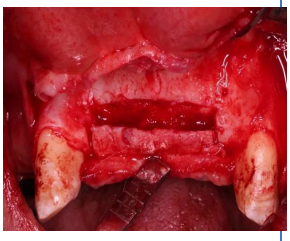
Figure 2 STL file exported from Anatomica Ai software as virtual design of the second surgical guide for achieving the planed segment movement and guided implant placement

Surgical procedure

Under local anesthesia, a full-thickness mucoperiosteal flap was elevated and the first guide (Osteotomies guide) was placed in position and fixed by four screws at the labial plate of bone. using cutting disc, A horizontal cut, was performed on the facial aspect of alveolar ridge followed by two vertical cuts at the distal and mesial ends of the horizontal cut 2mm away from teeth (Figure 3). The alveolar segment was mobilized while maintaining its palatal soft tissue attachment (Figure 4). The repositioning guide was subsequently fixed to achieve the planned vertical displacement and to minimize palatal tipping of the transported segment (Figure 5). Dental implants were inserted simultaneously through the surgical guide, engaging both the mobilized segment and basal bone to achieve primary stability.[5] In the control group, bovine-derived xenograft particles were mixed with saline and placed within the osteotomy gap. In the study group, the xenograft was mixed with RGD-functionalized hydrogel before placement (Figure 6). In both groups, the grafted area was covered with a collagen membrane and the wound was closed with tension-free sutures. Final restoration was loaded after 6 months (Figure 7-8).

Radiographic evaluation

Volumetric bone changes were assessed using segmentation analysis in Mimics Medical 21.0 software. For standardization, the right-to-left (R–L) line in the axial section was positioned at the most posterior point of the hard palate using a fixed anatomical landmark.[11] A threshold value of 300 HU was applied for all scans. The augmented bone segment was isolated using the region-growing, mask editing, and erase tools, followed by segmentation of the grafted area. The segmented volume was cropped mesial and distally to define the augmented region as an independent segment, and volumetric measurements were automatically calculated by the software in cubic centimeters (cm^3).[12] Assessments were performed on preoperative, immediate postoperative, 6-month, and 12-month CBCT scans, and the obtained volumetric data were recorded for statistical analysis (Figure 9-10-11-12).



[2] The Rainbow Scanner Prime is a digital dental scanning system manufactured by Dentium Co., Ltd., headquartered in Suwon.

Figure 3 Clinical photo showing horizontal and vertical cuts after first guide was removed. .

Figure 4 Clinical photo showing mobilization of separated segment in an occlusal direction.

Figure 5 Clinical photo showing the second guide was fixed in optimal position.

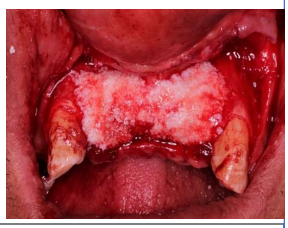


Figure 6 Clinical photo showing graft material packed as a gap-filling material in surgical site.

Figure 7 Clinical photo showing wound suturing using polyproline (4/0) non resorbable suturing material.

Figure 8 Final restoration 6 months after loading.

Figure 9 Preoperative measurement of bone segment volume.

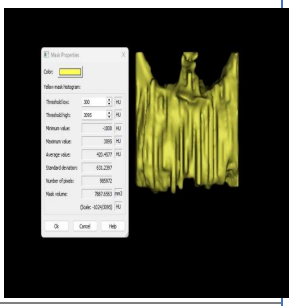


Figure 10 Immediate postoperative measurement of bone segment volume.

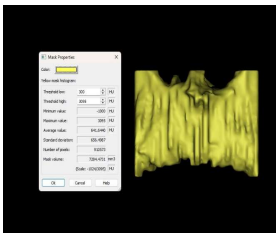


Figure 11 Measurement of bone segment volume at 6 months of follow up

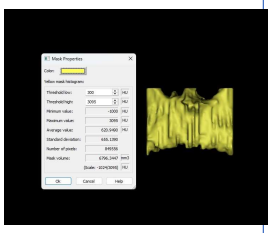


Figure 12 Measurement of bone segment volume at 12 months of follow up.

Results

Both groups achieved statistically significant volumetric bone gain (3.19 ± 0.89 to 5.39 ± 1.01 Cm^3 in control group and from 3.54 ± 0.62 to 5.13 ± 0.72 Cm^3 in study group) immediately postoperative. The changes were almost maintained through the follow-up periods. Between groups, no significant differences (P>0.05) were observed. (Table 1, figure 13).

Table X Volumetric bone changes by segmentation (Cm^3).

Time	G1 Mean ± SD	G2 Mean ± SD	Group effect *p*
Preoperative	3.19 ± 0.89	3.54 ± 0.62	0.173
Immediate post operative	5.68 ± 1.03*	5.62 ± 0.89*	0.925
After 6 months	5.43 ± 0.99*	5.26 ± 0.83*	0.750
After 12 months	5.39 ± 1.01*	5.13 ± 0.72*	0.626
Time effect *p*	0.000	0.001	
Interaction effect *p*			0.024

P<0.05: represents significant effect. *: represents a significant difference as compared to preoperative measurements.

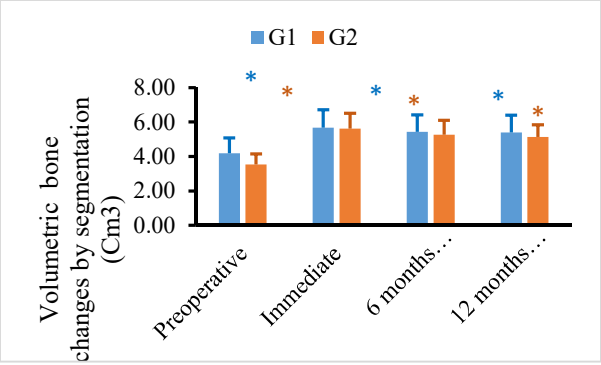


Figure 13 Volumetric bone changes by (Cm^3). Data is presented as mean ± standard deviation (SD). *: represents a significant difference as compared to preoperative measurements.

Discussion

Vertical ridge augmentation remains one of the most demanding procedures in implant dentistry because successful regeneration must be achieved in the absence of natural bony wall containment.[13] The present randomized clinical trial evaluated the effect of adding RGD-functionalized hydrogel to xenograft in conjunction with a computer-guided sandwich osteotomy technique and simultaneous implant placement for the treatment of maxillary vertical ridge deficiencies.

The main finding of the present study was that both treatment modalities resulted in significant volumetric bone gain compared with baseline values. In the control group, the mean bone volume increased from 3.19 ± 0.89 cm^3 preoperatively to 5.39 ± 1.01 cm^3 after 12 months, while the study group demonstrated an increase from 3.54 ± 0.62 cm^3 to 5.13 ± 0.72 cm^3. Moreover, the augmented volumes were largely maintained throughout the follow-up period, indicating favorable dimensional stability of the regenerated tissues.

These findings may be attributed to explanation support the effectiveness of the sandwich osteotomy technique as a predictable method for vertical ridge augmentation. Preservation of the vascular supply through maintenance of the palatal periosteal attachment may have contributed to the favorable healing and stability observed in both groups.[14]

The significant increase in bone volume observed immediately after surgery can be attributed to the vertical repositioning of the alveolar segment combined with placement of the interpositional graft material.[15] The slight reduction in volume detected during the healing period is consistent with the physiological remodeling process that follows bone augmentation procedures. Nevertheless, the limited volumetric reduction observed between the immediate postoperative and 12-month evaluations suggests that the computer-guided sandwich osteotomy technique provided stable long-term augmentation.[5]

These finding are in agreement with the systematic review of Roccuzzo et al[3]., who concluded that sandwich osteotomy is a reliable approach for vertical ridge augmentation with favorable implant related outcomes and limited volumetric resorption. Similarly, El-Zahwy et al.[4] reported significant vertical bone gain and acceptable dimensional stability when using interpositional grafting techniques for augmentation of anterior maxillary defects. The present findings further support the concept that maintaining vascularization of the mobilized segment enhances graft incorporation and reduces postoperative resorption.[16]

A notable finding of the current study was the absence of statistically significant differences between the xenograft-only group and the RGD-hydrogel group regarding volumetric bone changes. Although RGD peptides have been reported to enhance cell adhesion, proliferation, and osteogenic differentiation through integrin-mediated signaling pathways[17], these biological advantages were not translated into significantly greater volumetric augmentation within the 12-month observation period. One possible explanation is that volumetric measurements primarily reflect dimensional changes of the augmented area rather than the quality or maturity of the newly formed bone. Therefore, any biological effect of the RGD hydrogel may have occurred at the cellular or microstructural level without substantially affecting the overall graft volume.

Another explanation may be related to the dominant space-maintaining effect of the xenograft particles. Xenografts are characterized by slow resorption and long-term volumetric stability[2], which may have masked subtle differences attributable to the hydrogel component. Consequently, both groups demonstrated comparable volumetric outcomes despite differences in graft composition.

The use of computer-guided surgery may also have contributed substantially to the favorable outcomes observed in both groups. Previous studies have highlighted the potential for palatal rotation and tipping of the mobilized segment as a major limitation of conventional sandwich osteotomy procedures.[18] In the present study, the use of patient-specific surgical

guides allowed accurate osteotomy execution, controlled repositioning of the transported segment, and simultaneous implant placement according to the virtual treatment plan. This likely minimized surgical variability and improved the predictability of the augmentation procedure. These observations are consistent with the findings of Nazzal et al[5] who reported enhanced surgical accuracy and more controlled segment positioning when computer-guided sandwich osteotomy was used.

A limitation of the present study is the relatively small sample size and the reliance on volumetric radiographic measurements without histologic evaluation of bone quality. Furthermore, the follow-up period was limited to 12 months. Therefore, longer-term studies incorporating histomorphometric assessment and larger patient populations are recommended to further investigate the biological effects of RGD-functionalized hydrogels on bone regeneration.

conclusion

Within the limitations of this study, computer-guided sandwich osteotomy combined with simultaneous implant placement proved to be an effective approach for the treatment of maxillary vertical ridge deficiencies. The patient-specific guide resists the tension generated by the palatal soft tissues, thereby preventing palatal rotation and tipping of the transported segment. Both xenograft alone and xenograft mixed with RGD-functionalized hydrogel achieved significant and stable volumetric bone augmentation. However, the addition of RGD hydrogel did not result in a statistically significant volumetric advantage over xenograft alone during the 12-month follow-up period.

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